CLAIMS

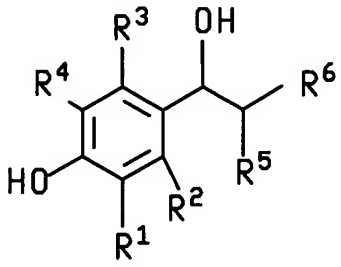
What is claimed is:

1. A method of treating sensorineural hearing loss in a mammal, which method comprises administering to the mammal an amount of an NR2B subunit selective NMDA antagonist, which amount is effective in treating sensorineural hearing loss.

2. A method according to claim 1, wherein the method is treating sensorineural hearing loss that is aminoglycoside-induced and/or of a genetic origin.

3. A method according to claim 1, wherein the sensorineural hearing loss is sound-induced.

4. A method according to claim 1, wherein the NR2B subunit selective NMDA receptor antagonist is a compound of the formula



,

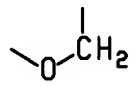
(I)

or a pharmaceutically acceptable acid addition salt thereof,

wherein:

(a) R^2 and R^5 are taken separately and R^1, R^2, R^3 and R^4 are each independently hydrogen, (C_1-C_6) alkyl, halo, CF_3, OH or OR^7 and R^5 is methyl or ethyl; or

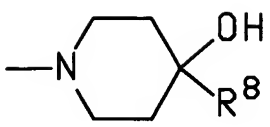
(b) R^2 and R^5 are taken together and are



,

forming a chroman-4-ol ring, and R^1, R^3 and R^4 are each independently hydrogen, (C_1-C_6) alkyl, halo, CF_3, OH or OR^7;

R^6 is



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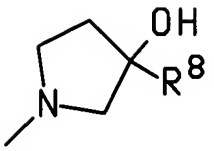
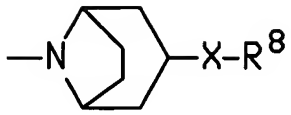


or



;

R^7 is methyl, ethyl, isopropyl or n-propyl;

R^8 is phenyl optionally substituted with up to three substituents independently selected from the group consisting of (C_1-C_6) alkyl, halo and CF_3;

X is O, S or $(CH_2)_n$; and

n is 0, 1, 2, or 3.

5. A method according to claim 1, wherein the NR2B subunit selective NMDA receptor antagonist is

(+)-(1S,2S)-1-(4-hydroxy-phenyl)-2-(4-hydroxy-4-phenylpiperidino)-1-propanol;

(1S,2S)-1-(4-hydroxy-3-methoxyphenyl)-2-(4-hydroxy-4-phenylpiperidino)-1-propanol;

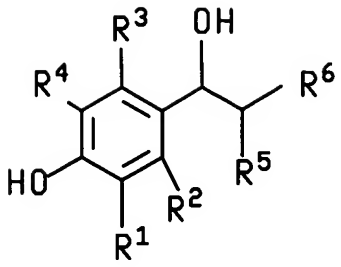
(3R,4S)-3-(4-(4-fluorophenyl)-4-hydroxypiperidin-1-yl)-chroman-4,7-diol;

a pharmaceutically-acceptable acid addition salt of one of said compounds; or

(1R*,2R*)-1-(4-hydroxy-3-methylphenyl)-2-(4-(4-fluorophenyl)-4-hydroxypiperidin-1-yl)-propan-1-ol-mesylate.

6. A method of treating neurological damage caused by epileptic seizures in a mammal, which method comprises administering to the mammal an amount of an NR2B subunit selective NMDA antagonist, which amount is effective in inhibiting neurological damage.

7. A method according to claim 6, wherein said NR2B subtype selective NMDA receptor antagonist is a compound of the formula



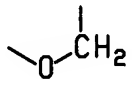
(I)

or a pharmaceutically acceptable acid addition salt thereof,

wherein:

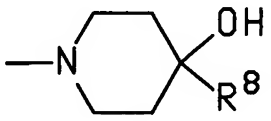
(a) R^2 and R^5 are taken separately and R^1, R^2, R^3 and R^4 are each independently hydrogen, (C_1-C_6) alkyl, halo, CF_3, OH or OR^7 and R^5 is methyl or ethyl; or

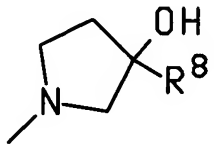
(b) R^2 and R^5 are taken together and are



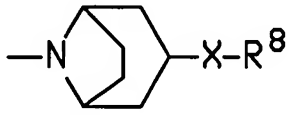
forming a chroman-4-ol ring, and R^1, R^3 and R^4 are each independently hydrogen, (C_1-C_6) alkyl, halo, CF_3, OH or OR^7;

R^6 is





or



;

R^7 is methyl, ethyl, isopropyl or n-propyl;

R^8 is phenyl optionally substituted with up to three substituents independently selected from the group consisting of (C_1-C_6) alkyl, halo and CF_3;

X is O, S or $(CH_2)_n$; and

n is 0, 1, 2, or 3.

8. A method according to claim 6, wherein the NR2B subunit selective NMDA receptor antagonist is (+)-(1S, 2S)-1-(4-hydroxy-phenyl)-2-(4-hydroxy-4-phenylpiperidino)-1-propanol;

(1S,2S)-1-(4-hydroxy-3-methoxyphenyl)-2-(4-hydroxy-4-phenylpiperidino)-1-propanol;

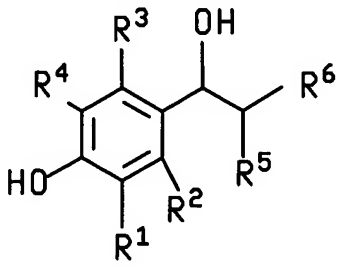
(3R,4S)-3-(4-(4-fluorophenyl)-4-hydroxypiperidin-1-yl)-chroman-4,7-diol;

a pharmaceutically-acceptable acid addition salt of one of said compounds; or

(1R*,2R*)-1-(4-hydroxy-3-methylphenyl)-2-(4-(4-fluorophenyl)-4-hydroxypiperidin-1-yl)-propan-1-ol-mesylate.

9. A method of treating neurological damage caused by neurotoxin poisoning in a mammal, which method comprises administering to the mammal an amount of an NR2B subunit selective NMDA antagonist, which amount is effective in inhibiting neurological damage.

10. A method according to claim 9, wherein the NR2B subunit selective NMDA receptor antagonist is a compound of the formula



,

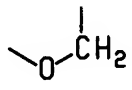
(I)

or a pharmaceutically acceptable acid addition salt thereof,

wherein:

(a) R^2 and R^5 are taken separately and R^1, R^2, R^3 and R^4 are each independently hydrogen, (C_1-C_6) alkyl, halo, CF_3, OH or OR^7 and R^5 is methyl or ethyl; or

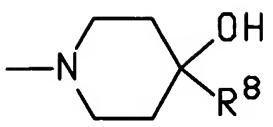
(b) R^2 and R^5 are taken together and are



,

forming a chroman-4-ol ring, and R^1, R^3 and R^4 are each independently hydrogen, (C_1-C_6) alkyl, halo, CF_3, OH or OR^7;

R^6 is



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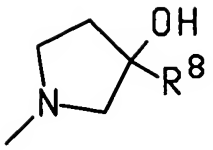

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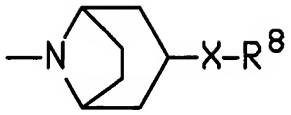


;

R^7 is methyl, ethyl, isopropyl or n-propyl;

R^8 is phenyl optionally substituted with up to three substituents independently selected from the group consisting of (C_1-C_6) alkyl, halo and CF_3;

X is O, S or $(CH_2)_n$; and

n is 0, 1, 2, or 3.

11. A method according to claim 9, wherein the NR2B subunit selective NMDA receptor antagonist is (+)-(1S, 2S)-1-(4-hydroxy-phenyl)-2-(4-hydroxy-4-phenylpiperidino)-1-propanol;

(1S,2S)-1-(4-hydroxy-3-methoxyphenyl)-2-(4-hydroxy-4-phenylpiperidino)-1-propanol;

(3R,4S)-3-(4-(4-fluorophenyl)-4-hydroxypiperidin-1-yl)-chroman-4,7-diol;

a pharmaceutically-acceptable acid addition salt of one of said compounds; or

(1R*,2R*)-1-(4-hydroxy-3-methylphenyl)-2-(4-(4-fluorophenyl)-4-hydroxypiperidin-1-yl)-propan-1-ol-mesylate.

12. A method of treating vision loss caused by neurodegeneration of the visual pathway in a mammal, which method comprises administering to the mammal an amount of an NR2B subunit selective NMDA antagonist, which amount is effective in treating vision loss caused by neurodegeneration of the visual pathway.

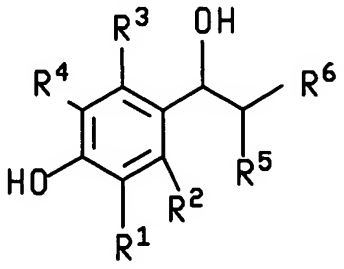
13. A method according to claim 12, wherein the neurodegeneration is caused by a stroke in the visual pathway.

14. A method according to claim 13, wherein the stroke is in the retina, optic nerve, and or occipital lobe.

15. A method according to claim 12, wherein the neurodegeneration is caused by a neurodegenerative disease, such as macular degeneration.

16. A method according to claim 15, wherein the neurodegeneration comprises retinal degeneration caused by glaucoma.

17. A method according to claim 12, wherein the NR2B subunit selective NMDA receptor antagonist is a compound of the formula



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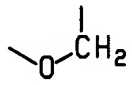
(I)

or a pharmaceutically acceptable acid addition salt thereof,

wherein:

(a) R^2 and R^5 are taken separately and R^1, R^2, R^3 and R^4 are each independently hydrogen, $(C_1\text{-}C_6)$ alkyl, halo, CF_3, OH or OR^7 and R^5 is methyl or ethyl; or

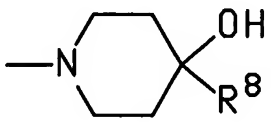
(b) R^2 and R^5 are taken together and are



,

forming a chroman-4-ol ring, and R^1, R^3 and R^4 are each independently hydrogen, $(C_1\text{-}C_6)$ alkyl, halo, CF_3, OH or OR^7;

R^6 is



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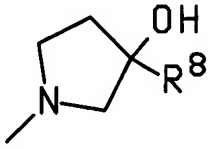

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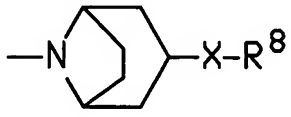


;

R^7 is methyl, ethyl, isopropyl or n-propyl;

R^8 is phenyl optionally substituted with up to three substituents independently selected from the group consisting of $(C_1\text{-}C_6)$ alkyl, halo and CF_3;

X is O, S or $(CH_2)_n$; and

n is 0, 1, 2, or 3.

18. A method according to claim 12, wherein the NR2B subunit selective NMDA receptor antagonist is

(+)-(1S,2S)-1-(4-hydroxy-phenyl)-2-(4-hydroxy-4-phenylpiperidino)-1-propanol;

(1S,2S)-1-(4-hydroxy-3-methoxyphenyl)-2-(4-hydroxy-4-phenylpiperidino)-1-propanol;

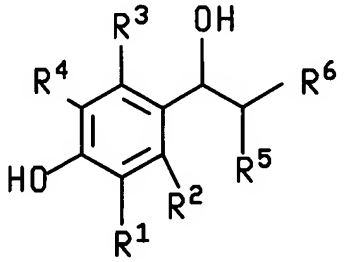
(3R,4S)-3-(4-(4-fluorophenyl)-4-hydroxypiperidin-1-yl)-chroman-4,7-diol;

a pharmaceutically-acceptable acid addition salt of one of said compounds; or

(1R*,2R*)-1-(4-hydroxy-3-methylphenyl)-2-(4-(4-fluorophenyl)-4-hydroxypiperidin-1-yl)-propan-1-ol-mesylate.

19. A method of treating multi-system atrophy in a mammal, which method comprises administering to the mammal an amount of an NR2B subunit selective NMDA antagonist, which amount is effective in treating multi-system atrophy.

20. A method according to claim 19, wherein the NR2B subunit selective NMDA receptor antagonist is a compound of the formula



,

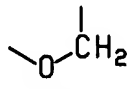
(I)

or a pharmaceutically acceptable acid addition salt thereof,

wherein:

(a) R^2 and R^5 are taken separately and R^1, R^2, R^3 and R^4 are each independently hydrogen, (C_1-C_6) alkyl, halo, CF_3, OH or OR^7 and R^5 is methyl or ethyl; or

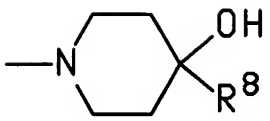
(b) R^2 and R^5 are taken together and are



,

forming a chroman-4-ol ring, and R^1, R^3 and R^4 are each independently hydrogen, (C_1-C_6) alkyl, halo, CF_3, OH or OR^7;

R^6 is



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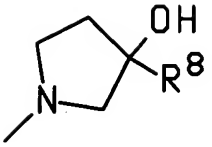
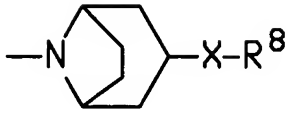


or



;

R^7 is methyl, ethyl, isopropyl or n-propyl;

R^8 is phenyl optionally substituted with up to three substituents independently selected from the group consisting of (C_1-C_6) alkyl, halo and CF_3;

X is O, S or $(CH_2)_n$; and

n is 0, 1, 2, or 3.

21. A method according to claim 19, wherein the NR2B subunit selective NMDA receptor antagonist is (+)-(1S, 2S)-1-(4-hydroxy-phenyl)-2-(4-hydroxy-4-phenylpiperidino)-1-propanol;

(1S,2S)-1-(4-hydroxy-3-methoxyphenyl)-2-(4-hydroxy-4-phenylpiperidino)-1-propanol;

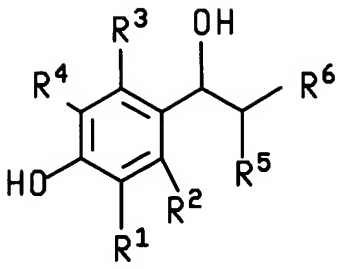
(3R,4S)-3-(4-(4-fluorophenyl)-4-hydroxypiperidin-1-yl)-chroman-4,7-diol;

a pharmaceutically-acceptable acid addition salt of one of said compounds; or

(1R*,2R*)-1-(4-hydroxy-3-methylphenyl)-2-(4-(4-fluorophenyl)-4-hydroxypiperidin-1-yl)-propan-1-ol-mesylate.

22. A method of treating non-vascular headache in a mammal, which method comprises administering to the mammal an amount of an NR2B subunit selective NMDA antagonist, which amount is effective in treating non-vascular headache.

23. A method according to claim 22, wherein the NR2B subunit selective NMDA receptor antagonist is a compound of the formula



,

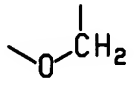
(I)

or a pharmaceutically acceptable acid addition salt thereof,

wherein:

(a) R^2 and R^5 are taken separately and R^1, R^2, R^3 and R^4 are each independently hydrogen, (C_1-C_6) alkyl, halo, CF_3, OH or OR^7 and R^5 is methyl or ethyl; or

(b) R^2 and R^5 are taken together and are



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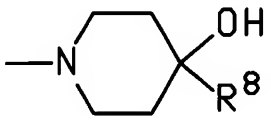
forming a chroman-4-ol ring, and R^1, R^3 and R^4 are each independently hydrogen, (C_1-C_6) alkyl, halo, CF_3, OH or OR^7;

R^6 is



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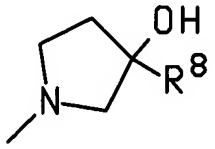
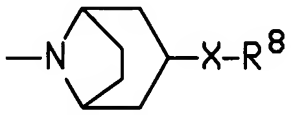


or



;

R^7 is methyl, ethyl, isopropyl or n-propyl;

R^8 is phenyl optionally substituted with up to three substituents independently selected from the group consisting of (C_1-C_6) alkyl, halo and CF_3;

X is O, S or $(CH_2)_n$; and

n is 0, 1, 2, or 3.

24. A method according to claim 22, wherein the NR2B subunit selective NMDA receptor antagonist is (+)-(1S, 2S)-1-(4-hydroxy-phenyl)-2-(4-hydroxy-4-phenylpiperidino)-1-propanol;

(1S,2S)-1-(4-hydroxy-3-methoxyphenyl)-2-(4-hydroxy-4-phenylpiperidino)-1-propanol;

(3R,4S)-3-(4-(4-fluorophenyl)-4-hydroxypiperidin-1-yl)-chroman-4,7-diol;

a pharmaceutically-acceptable acid addition salt of one of said compounds; or

(1R*,2R*)-1-(4-hydroxy-3-methylphenyl)-2-(4-(4-fluorophenyl)-4-hydroxypiperidin-1-yl)-propan-1-ol-mesylate.